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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,109	06/22/2006	Kenichiro Kosai	55801-003US1	8348

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
06/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/584,109	KOSAI ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/22/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 03/03/08 has been acknowledged and fully considered.

Claims 1-27 are pending and are examined in this office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Kinsella (US 7060433 B1, 2006). The scope of invention as claimed herein encompasses an expression vector containing a CD9 gene. Kinsella teaches an expression vector comprising a CD9 gene, wherein the expression vector is retroviral vector. Thus given the broadest reasonable interpretation the cited art clearly anticipates the product as claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating myocardial infarction in a heart by directly administering to cardiac muscles adenoviral vectors encoding HB-EFG and CD9 (Ad.HB-EGF+Ad.CD9), does not reasonably provide enablement for a method for preventing or treating any heart disease by expressing CD9 gene in heart via any and all means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature Of Invention:

The instant invention relates to a method for heart gene therapy.

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of invention as claimed encompasses a method for preventing or treating any heart disease (i.e. ischemic heart disease, cardiomyopathy, hypertensive heart diseases, valvular disease, congenital heart diseases and myocarditis arrhythmia. cardiac hypertrophy, tachycardia etc) by expressing CD9 gene in heart via any and all means (i.e. using any and all kinds of substance or viral or non-viral vectors, wherein the vectors are administered via any and all routes of administration. At very best the specification teaches a method for treating myocardial infarction in a heart by directly administering to cardiac muscles adenoviral vectors encoding HB-EFG and CD9 (Ad.HB-EGF+Ad.CD9). The specification as filed fails to disclose preventing or treating any heart disease via method as broadly claimed herein.

State Of Art And Predictability:

The scope of the instant invention encompasses genetic modification of a cell in-vivo, therefore the invention falls in the realm of gene therapy. The gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations. (see Raper, SURGERY, 137(5):487-492, 2005; Kimmelman, BMJ, 220:79-82, 2003; Juengst, BMJ, 326:1410-1411, 2003; Wolf, NAT. BIOTECHNOL.

20:768-769, 2002; Rosenberg et al, SCIENCE 287:1751, 2000; Donsante et al, SCIENCE, 317:477, 2007; Couzin et al, SCIENCE 307:1028, 2005; Touchette, NAT. MED. 2(1):7-8, 1996).

The US Food and Drug Administration (FDA) and the NIH responded to widespread concern about risks, especially after the 1999 death of teenager in a phase I clinical trial. Many laboratories were shut down, public meetings were held, reviews and investigations commissioned and administrative changes have been put in place to deal with the crisis. But the troubles run deep within the heartland of biomedical science, where the most important concern remains the issue of *safety*. Gene therapy targets diseases based on the transfer of genetic material into an individual, rather than a drug. It uses genes as the therapeutic agent, and it is qualitatively very different from other forms of treatment.

Gene therapy is targeted at virtually every ill known to human beings, especially those inhabiting the first world, including pain relief, cosmetic hair replacement and muscle building. Massive investment has gone in but no clinical efficacy has ever been proven, despite anecdotal claims of success. Most studies have neglected to include well-defined biochemical or clinical end points that would clearly indicate whether the therapy is having a desired effect. The Recombinant DNA Advisory committee (RAC) also emphasized that expectation of current gene therapy protocols have been over sold without any apparent success. The advisory panel further emphasized the need for a greater understanding of an underlying mechanism associated with etiology of the disease in context.

Furthermore, gene transfer frequency is extremely low and results of gene therapy protocols rely on qualitative rather that quantitative assessments of gene transfer and expression. The panel concluded "only a minority of clinical studies, illustrated by some gene marking experiments, have been designed to yield useful basic information" [as these at least track the fate of the genetic vector]. The report states that there is "concern at the overselling of results of laboratory and clinical studies by investigators and their sponsors, either academic, federal, or industrial, leading to the

widespread perception that gene therapy is further developed and more successful that it actually is".

The NIH expert panel found that all gene transfer vectors are ineffective and it is not understood how they interact with the host. Basic studies of disease pathology and physiology have not been done, which are critical for designing treatment. Gene transfer frequency is extremely low and results of gene therapy protocols rely on qualitative rather that quantitative assessments of gene transfer and expression. There are no controls, and biochemical or disease endpoints are not define

In instant case considering the etiologies associated with varieties of heart diseases, state of the art at the time of filing and limited amount of guidance provided in the specification as filed, it is highly unpredictable that one skilled in the art would be able to make and use the invention commensurate in scope with instant claims. For example the specification as filed fails to disclose that administration of an expression vector encoding CD9 gene alone is capable of eliciting the asserted therapeutic effects in any heart diseases. Furthermore CD9 is a member of the tetraspanins, and has been shown to be involved in a variety of cellular activities such as migration, proliferation, and adhesion; and is also known that CD9 can associate with variety of other proteins (see Murayama et al 1: J Cell Physiol. 216(1):135-43, 2008)

One of the greatest challenges facing gene therapy is the efficient transfer and stable expression of transgene in appropriate tissues. It has been difficult to predict the efficiency and out come of transduced therapeutic genes because various factors govern the expression and/or therapeutic potential of transduced genes in vivo. The transduction of target cells represents the first critical step in gene therapy, which not only depends upon the type of target cells but also on the choice and/or characteristics of delivery vectors. Although the retroviral vectors are the vectors of choice, they require target cells to be in cycling state for the successful delivery of gene of interest. On the other hand vector comprising DNA viruses and liposome coated DNA have been used to transduce non dividing cells but this results in a transient expression due to non-integration of transgenes in host cells.

Furthermore, in-vitro gene transfer studies are not predictive of in-vivo gene therapy because gene transfer frequency is much higher in-vitro models where most of cells are under going rapid cell division, which is quite not the case in-vivo environment.

In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacles to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets.

In addition there exists an uncertainty about the degree to which a vector's genetic material may integrate into the host genome extends to most types of gene therapy trials. Scientists are also unsure how an insertion could affect a patient, and worry cancer could occasionally be triggered, such as occurred various trials involving gene therapy. Although, the gene therapy holds much promise to come, the success will only be achieved through continued rigorous research on the most fundamental mechanisms that contribute to a genetic disease along with the pathogenesis of the disease, gene delivery and gene expression in animals.

In instant case preventing or treating any heart disease by expressing CD9 gene in heart via any and all means is not considered routine in the art and without sufficient enabling disclosure the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sumesh Kaushal/
Primary Examiner, Art Unit 1633

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